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A current approach to acute mediastinitis

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ABSTRACT

Acute mediastinitis is still among the major causes of high mortality despite advances in antibiotic therapies, intensive care support, and novel diagnostic techniques. Mediastinitis may develop due to esophageal perforation, by a downward spread of neck infection, or after cardiothoracic surgery. While computed tomography is the most preferred imaging technique in diagnosis, broad-spectrum antibiotic therapy and surgical debridement are the mainstay of the treatment. It is essential to combine multiple interventions, such as appropriate antimicrobial prophylaxis, minimization of contamination, elimination of preoperative nasal *S. aureus* carriage, and the adoption of relevant surgical techniques, to prevent particularly postoperative mediastinitis.

Keywords: Acute mediastinitis, antibiotic therapy, surgical debridement

INTRODUCTION

Acute mediastinitis is a rare but severe and progressive condition characterized by diffuse inflammation in the mediastinum. The mediastinum is an anatomically closed intrathoracic cavity housing the heart, great vessels, trachea, esophagus, thymus, and lymph nodes. Due to the well-vascularized fat tissue in this space and the proximity of vital organs, advanced cases usually present with fever and tachycardia, accompanied by hypotension, multiple organ failure, rapid progression to sepsis, and the need for intensive care.[1,2]

Mediastinitis may develop due to esophageal perforation, by a downward spread from the neck (descending necrotizing mediastinitis (DNM)), or postoperatively (deep sternal surgical wound infection (DSWI) after sternotomy). At the same time, it can spread through the bloodstream from the pleural cavity or focus on infection in another region in the presence of empyema.[3]

EPIDEMIOLOGY, DEFINITIONS, AND RISK FACTORS

Acute mediastinitis is still among the major causes of high mortality despite advances in antibiotic therapies, intensive care support, and novel diagnostic techniques. The global mortality rate varies between 19-47% depending on the underlying cause. The condition is seen in both sexes but affects males one-sixth more. Its incidence increases in the third, fourth, and fifth decade of life, and advancing age contributes to mortality. About 60% of acute mediastinitis is due to complications following cardiac operations. While esophageal perforations account for 25-31% of mediastinitis, the remaining is mainly caused by oropharyngeal infection.[4]

POSTOPERATIVE MEDIASTINITIS

It is the condition in which the mediastinum becomes infected during DSWI following sternotomy. According to the Centers for Disease Control and Prevention (CDC), diagnosis is made upon fever >38.0°C, chest pain, purulent discharge in the surgical site in the presence of sternal instability, mediastinal widening in radiological imaging, microorganisms in fluid and tissue samples from the mediastinum, or histopathological classification of mediastinitis in tissue samples from the mediastinum.[5]

The sternal surgical wound infection is defined as a superficial infection when the infection affects the dermis and subcutaneous tissue or a DSWI when it extends below the sternum and anterior mediastinum. It was previously reported that DSWI occurs between 0.5% - 2.2% of patients following cardiac surgery and leads to 14% mortality. Intraoperative wound contamination from the patient's endogenous flora may be the most apparent factor for postoperative mediastinitis. The contamination occurs in almost all patients due to the prolonged time the sternotomy remains open during cardiac surgery. The degree, type, and host factors (nutrition, immunological status) of contamination determine the risk of infection. Providing that suitable conditions are ensured during surgery, the contamination causes infection in only a small number of patients.[6,7] The causative agent is usually monomicrobial, and what is isolated most prevalently is *Staphylococcus aureus*. Gram-negative bacilli, coagulase-negative staphylococci, and streptococci can also be detected as agents. Although surgical wound infection may occur months later in some cases, it emerges within the first 30 days postoperatively among the majority.

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Preoperative, intraoperative, and postoperative risk factors for postoperative mediastinitis have already been defined. Preoperative risk factors are known to be nasal colonization with *Staphylococcus aureus*, diabetes mellitus (DM) or perioperative hyperglycemia, obesity, heart failure and left ventricular dysfunction, smoking, previous cardiac surgery, an end-stage renal disease requiring hemodialysis, chronic obstructive pulmonary disease, using an intra-aortic balloon pump, and using an electric razor instead of a razor blade for hair removal. While intraoperative risk factors are emergency surgery, using an internal mammary artery graft, prolonged perfusion and aortic clamp time, and prolonged surgical procedure (> 5 hours), postoperative risk factors are the need for mechanical ventilation, prolonged need for an intensive care unit, and poor glycemic control.[3,6,8-10]

DESCENDING NECROTIZING MEDIASTINITIS

DNM originates with direct extension of odontogenic (36-47%), pharyngeal (33-45%), and cervical (15%) infections from the deep facial, retropharyngeal, and peritracheal spaces to the tissue planes in the mediastinum. Its most prevalent sources are peritonsillar, parapharyngeal, dental, or odontogenic abscesses. In addition to prevalent infections (e.g., tonsillitis, epiglottitis, pharyngitis), it can also emerge due to primary neck infections, cervical lymphadenitis, suppurative thyroiditis, parotitis, and traumatic endotracheal intubation. The retropharyngeal space opens directly into the posterior mediastinum, accounting for the spread of 70% of oropharyngeal infections. If not treated early and appropriately, it may cause multiple organ failure, sepsis, and mortality (11-40%). Normal flora members of the oral cavity, upper respiratory tract, and ear mucosal surfaces are responsible for the infection; thus, it is typically polymicrobial. On the other hand, the most prevalently isolated agents are known to be *Streptococcus* spp., *S. aureus*, and anaerobes (*Peptostreptococcus* spp., *Fusobacterium nucleatum*, *Prevotella* spp.). In addition to these pathogens, *Pseudomonas aeruginosa*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis* may be causative agents in autogenic or sinus-borne infections.[4] Diagnostic criteria proposed by Estrera et al.[11] include clinical signs of severe infection, characteristic findings on radiological imaging, intraoperative or postmortem detection of necrotizing mediastinal infection, and a relationship between necrotizing mediastinitis and oropharyngeal or cervical infection. Immunosuppression, DM, oral glucocorticoids, peripheral arterial disease, and reduced tissue oxygenation due to cardiac and respiratory failure are major risk factors for DNM.

MEDIASTINITIS FOLLOWING ESOPHAGEAL PERFORATION

The passage of colonized microorganisms, salivary, esophageal, and gastric contents into the mediastinum due to any disruption of the esophageal wall integrity results in mediastinitis. More than half of esophageal perforations occur iatrogenically during endoscopic procedures. While this probability may be negligible during simple endoscopy (< 0.5%), it increases (2-6%) when performing dilatation or using a rigid esophagoscope for achalasia. Perforation is more likely in sites with physiological stenosis (e.g., the cricopharyngeal muscle and esophagogastric junction). Spontaneous perforation (Boerhaave's syndrome) accounts for up to 15% of all perforations, and such patients usually have a history of alcoholism and/or gastric and duodenal ulcers. Its other less prevalent causes are trauma, surgical anastomosis, and malignancy.[12,13] The agents in mediastinitis following esophageal perforation are the members of the normal oropharynx flora (streptococci, anaerobes, *Neisseria* spp., *Haemophilus* spp.); nevertheless, the patient's immunosuppression, intubation, enteral nutrition, and recent antibiotic exposure may change this profile. In these cases, the flora members are replaced by gram-negative bacteria, *S. aureus*, and *Candida* spp., and it is expected that these microorganisms will emerge as agents.[14]

CLINICAL MANIFESTATIONS

The clinical findings of mediastinitis vary by the underlying cause; fever, chills, and tachycardia are usual findings of mediastinitis. Pain can be masked, particularly among intensive care patients, and throat infection and trismus may accompany the clinical picture. Moreover, symptoms of systemic inflammatory response syndrome (SIRS) may be observed depending on the underlying etiology and patient characteristics. Increased inflammatory parameters in laboratory tests and elevated leukocyte count, C-reactive protein, and procalcitonin levels are also prevalent. Thrombocytopenia or disseminated intravascular coagulation may develop in association with sepsis. For appropriate antimicrobial therapy, fluid and tissue samples from the infected sternum or mediastinum during surgical debridement or abscess and blood cultures may need to be requested. Pleural fluid and bronchoalveolar lavage samples may also be required in patients in advanced stages. Superficial wound cultures should be carefully evaluated as they can be an indicator of colonization.

RADIOLOGICAL IMAGING

A simple posteroanterior chest radiograph may demonstrate the presence of air between the sternal edges. The displacement of one or more sternal wires may be an indirect indication of separation of the sternum.[15] Computed tomography (CT) should be performed on the neck and chest to confirm the diagnosis. In addition to being rather sensitive for diagnosis, CT can also provide insights about the underlying cause and the extent of the infection, helping plan appropriate surgical intervention. Sternal separation on CT, the presence of free air under the sternum, and mediastinal fluid collections indicate the presence of mediastinitis. Despite the high sensitivity, a differential diagnosis may not be possible in postsurgical mediastinitis because of postoperative inflammatory changes. In this case, repeat CT or scintigraphy may be needed to assess progression.[16]

TREATMENT

Relevant empirical antibiotic therapy should be initiated as soon as after collecting blood samples, and current surgical techniques should be considered in patients with suspected or diagnosed mediastinitis. Control of the focus of infection

and surgical debridement are the mainstay of the treatment. Clinical progression may vary depending on rapid diagnosis, adequate treatment, underlying cause, and comorbidities.[17]

Broad-spectrum intravenous antibiotic therapy should be initiated in mediastinitis associated with a sternal surgical wound infection after collecting cultures for microbiological identification and antibiogram. Empirical antibiotic therapy should include methicillin-susceptible *S. aureus*, skin flora members, and gastrointestinal gram-negative bacteria. Since methicillin-resistant coagulase-negative staphylococci and MRSA are prevalent in addition to broad-spectrum beta-lactam penicillin (e.g., piperacillin-tazobactam), vancomycin should be added in the treatment until obtaining culture results. Treatment should be planned for two-six weeks by evaluating adequate debridement and osteomyelitis.

Many different approaches have been described in the surgical treatment of post-sternotomy mediastinitis: reconstruction with revision (with open dressing), primary closure, closed irrigation, negative pressure wound therapy, and reconstruction with vascularized soft tissue (omentum, pectoral muscle) flap. Despite no consensus on the most appropriate surgical approach, there is at least some agreement on the necessity of wound debridement. Primary closure and tertiary closure or delayed primary closure are the two most commonly preferred techniques of wound closure. The wound is left open for follow-up and treatment following debridement and closed after a few days.[3]

Broad-spectrum intravenous antibiotic therapy, including aerobic and anaerobic bacteria, should be started for DNM. Intensive care monitoring may be required for optimal treatment in the presence of severe sepsis or septic shock. After treatment of the pharyngeal or dental focus and airway management, rapid and adequate neck and mediastinal drainage should be performed. Airway compression due to inflammation and edema is prevalent, and early tracheotomy ensures airway safety. Rapid surgical intervention, including systematic debridement and opening of the fascial spaces, is required to prevent the severe complications of persistent and progressive disease.[18] The surgical strategy is decided on by the extent of the disease. While cervicectomy and transcervical drainage may be adequate for localized infections in the upper mediastinum (above the carina), additional subxiphoid drainage should be considered in localized disease and stable cases where the infection progresses downward. More aggressively, median sternotomy and complete removal of necrotic tissue may also be required. Although posterolateral thoracotomy is acknowledged as a standard approach, the posterior mediastinum can be accessed in selected patients with the help of the clamshell approach, uni/bilateral thoracotomy, or uni/bilateral video-assisted thoracoscopic surgery (VATS). Yet, re-operation rates were previously reported to be high in research where less invasive approaches, such as subxiphoid drainage and VATS, were adopted. As a rule of thumb, the optimal treatment is radical surgical debridement of the affected tissue (e.g., pericardial adipose tissue and thymus) with an open thoracic approach.[19] Overall, each method bears potential pros and cons. Therefore, the surgical approach should be carefully chosen by the patient's condition, the extent of the disease, and the surgeon's experience to reduce the rates of complications, re-operation, and mortality.[19,20] The patient's oral intake should be discontinued, and aggressive intravenous fluid replacement and broad-spectrum antibiotic therapy covering aerobic and anaerobic bacteria should be started in mediastinitis developing due to esophageal peroration. Antifungal coverage may be required in immunosuppressive patients or those with prior broad-spectrum antibiotic use. The treatment should be assisted with proton pump inhibitors to prevent acid reflux. Planning an optimal treatment may require a multidisciplinary approach considering the patient's condition and the dynamics of the esophageal perforation.[21,22]

Primary repair of the perforation site is required in all cases, but the repair is more likely to be disrupted in patients diagnosed after 72 hours. Yet, the repair may not be convenient for patients with invisible or inaccessible cervical perforations, diffuse mediastinal necrosis or perforations that cannot be approximated, esophageal malignancies, end-stage achalasia, or clinical instability.[23]

Non-operative Approach

It can be preferred in minor iatrogenic or traumatic injuries with minimal extraluminal contamination, usually diagnosed at the time of perforation during or shortly after the procedure. The most critical aspect of the non-operative approach is careful patient selection. Iatrogenic cervical perforations are often deemed suitable for non-operative management. Endoscopic stent placement/vacuum-assisted closure and percutaneous or surgical intervention may be necessary for larger leaks.[24]

Prophylaxis

In the perioperative period, it is often aimed to minimize contamination and optimize the immune response in any applications to prevent surgical wound infection. Preoperative screening for nasal carriage of MRSA should be adopted to avoid virulent pathogen contamination. A five-day topical mupirocin treatment is recommended for the elimination of carriage. A single dose of beta-lactam antibiotic should be administered for cardiac surgical antibiotic prophylaxis in areas with a low incidence of MRSA. For beta-lactam allergy, prophylaxis may need to be ensured with vancomycin. While cefazolin should be given within 60 minutes of skin incision, vancomycin should be administered as an infusion for at least one hour. Nevertheless, antibiotic prophylaxis should not be applied for longer than 48 hours in the postoperative period. Skin antisepsis and perioperative hyperglycemia control should be ensured with povidone-iodine or chlorhexidine gluconate.[25]

Careful median sternotomy, bleeding control, and limited dissection are necessary to prevent infection during the operation. Paramedian sternotomy is associated with postoperative sternal instability. Sternal instability and dissociation may be an indication of surgical wound infection and may also end up with bacterial overgrowth. Rigid mechanical fixation of the sternal edges reduces the infection rate. Many novel techniques (e.g., surgical plate, wire) are utilized, but prospective controlled research is needed to demonstrate that these methods can reduce the rate of mediastinitis. When comparing the use of the bilateral internal mammary artery (BIMA) with the use of only the left internal mammary artery (LIMA), it was previously reported that the use of BIMA reduces the vascularization of the sternum and increases the risk of surgical wound infection. However, the subsequent research concluded that the increase in this rate is often significant in diabetic patients. Skeletonized IMA dissection is recommended in the case of DM or when BIMA is utilized.[26-28]

CONCLUSION

Acute mediastinitis is a clinical condition with a high mortality rate mostly occurs as a complication of a cardiothoracic surgical procedures.Prevention of surgical site infection depends on compliance with infections control measures and appropriate surgical intervention. Rapid diagnosis and eligible treatment approach should be implemented for reducing mortality.

ETHICAL DECLARATIONS

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